ISRCTN96178713 https://doi.org/10.1186/ISRCTN96178713

Stopping or continuing blood thinners after stroke at young age without a known cause: STOP trial

Submission date 11/07/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 17/09/2024	**Overall study status** Ongoing	
Last Edited 11/08/2026	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
In the Netherlands, 100,000 patients live with the long-term consequences of a TIA or ischaemic stroke at a young age (18-49 years old). The majority of these patients will use lifelong blood thinners (for example clopidogrel). This treatment strategy is based on studies among people with stroke due to atherosclerosis, who were on average 65 years of age. It is unknown whether lifelong use of blood thinners is effective for young people with TIA or ischaemic stroke as it is in elderly people, particularly in patients without a known cause for their stroke (cryptogenic stroke). Yet, young patients are exposed to blood thinners for decades with an increased risk of serious bleeding. It has never been established whether the benefits of blood thinners outweigh the risks for young patients, particularly in patients without atherosclerosis. The STOP trial aims to investigate whether blood thinners can safely be stopped three or more years after a TIA or ischemic stroke without a known cause at a young age.

Who can participate?
Patients who had a TIA or ischaemic stroke at the age of 18-49 years, for which the treating neurologist did not find a cause. The TIA or ischaemic stroke should have taken place at least 3 years before inclusion and participation in the study and patients should not have experienced a recurrent stroke or myocardial infarction afterwards.

What does the study involve?
Patients are randomly allocated to two groups: group 1 stops taking blood thinners, and group 2 continues taking blood thinners. Patients are requested to fill in a questionnaire each year. The study will run for 5 years.

What are the possible benefits and risks of participating?
Patients who stop using blood thinners have a lower risk of serious bleeding complications. In addition, stopping antiplatelet therapy provides convenience for patients who don’t have to take daily antiplatelet medication.

Patients who continue to use blood thinners have a risk of serious bleeding (for example bleeding from the gut or even bleeding in the brain). We expect that the risk of a recurrent stroke or myocardial infarction is similar for patients who stop or continue blood thinners. However, there might be a very small increased risk of a recurrent stroke or myocardial infarction among patients who stop blood thinners.

Where is the study run from?
The Radboud University Medical Center Nijmegen, the Netherlands

When is the study starting and how long is it expected to run for?
Recruitment is planned to start in october 2024 and run for two years

Who is funding the study?
The Netherlands Organisation for Health Research and Development

Who is the main contact?
Prof. Frank-Erik de Leeuw, FrankErik.deLeeuw@radboudumc.nl

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Frank Erik De Leeuw

ORCID ID
https://orcid.org/0000-0003-2221-3026

Contact details
Geert Grooteplein Zuid 10
Nijmegen
Netherlands
6500 HB
+31243098289
FrankErik.deLeeuw@radboudumc.nl

Additional identifiers

Clinical Trials Information System (CTIS)
2024-513092-40-00

Protocol serial number
114180, ZonMw Subsidy decision on file number: 10140252210002

Study information

Scientific Title
Stopping or continuing platelet inhibitors after cryptogenic stroke at young age: STOP trial

Acronym
STOP trial

Study objectives
Discontinuaton of antiplatelet drugs is non-inferior to continuation of antiplatelet durgs, three or more years after a cryptogenic stroke at young age

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/11/2024, METC Oost Nederland (Geert Grooteplein Zuid 10, Nijmegen, 6500 HB, Netherlands; +31243613154; metcoost-en-cmo@radboudumc.nl), ref: None provided

Primary study design
Interventional

Study design
Multicenter randomized non-inferiority trial

Study type(s)
Safety, Treatment

Health condition(s) or problem(s) studied
Patients with cryptogenic stroke at the age of 18-49 years

Interventions
Discontinuation of antiplatelet therapy.
The intervention is the discontinuation of oral daily antiplatelet therapy (clopidogrel 75mg once daily or acetylsalicylic acid 80mg once daily, with or without dipyridamole 200mg twice daily). The comparator is the continuation of antiplatelet therapy according to standard care. There is no specific trial drug manufacturer. Patients will be randomly allocated 1:1 by an external web-based system to the intervention or comparator arm.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Clopidogrel, acetylsalicylic acid, dipyridamole

Primary outcome(s)
Primary efficacy outcome:
1. A composite endpoint of major vascular events, defined as TIA with imaging confirmation, stroke, myocardial infarction, or death from vascular causes measured using a digital questionnaire or telephone follow-up and verified with medical records with annual follow-up for five years
Primary safety outcome:

2. Major bleeding, according to the International Society for Thrombosis and Haemostasis criteria, measured using a digital questionnaire or telephone follow-up and verified with medical records with annual follow-up for five years

Key secondary outcome(s)
The following secondary outcome measures are assessed using digital questionnaires or telephone follow-up with annual follow-up for five years:
1. Disability measured using the modified Ranking Scale
2. Quality of life measured using EQ-5D-5L
3. All cause mortality

Completion date
01/11/2032

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 06/08/2026:
1. First-ever ischaemic stroke, or TIA with evidence of ischaemia on imaging, 3-12 years before study participation
2. Age 18-49 years old at the time of TIA/ischaemic stroke
3. Cryptogenic aetiology, defined as no other aetiology after standard work-up according to national and international guidelines for young stroke (imaging of the brain (CT-scan or MRI-scan) and cervical arteries (CTA, MRA or carotid ultrasound), routine blood tests (complete blood count), ECG, at least 24 hours cardiac rhythm monitoring and transthoracic/transesophageal echocardiography).

Previous key inclusion criteria:
1. First-ever ischaemic stroke, or TIA with evidence of ischaemia on imaging, 3-10 years before study participation
2. Age 18-49 years old at the time of TIA/ischaemic stroke
3. Cryptogenic aetiology, defined as no other aetiology after standard work-up according to national and international guidelines for young stroke (imaging of the brain (CT-scan or MRI-scan) and cervical arteries (CTA, MRA or carotid ultrasound), routine blood tests (complete blood count, erythrocyte sedimentation rate, CRP, antiphospholipid antibodies, ECG, at least 24 hours cardiac rhythm monitoring and transthoracic/transesophageal echocardiography).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit

65 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. History of MI, coronary revascularisation or documented peripheral arterial disease
2. Other indication for antiplatelet therapy
3. Indication for oral anticoagulants or low molecular weight heparin
4. Recurrent ischaemic event at any time after the index event
5. Any stenosis of intracranial or cervical artery at time of stroke
6. Two or more risk factors for atherosclerotic disease prior to the index event, according to the following definitions:
6.1. Arterial hypertension (treated or known blood pressure before stroke >140/90 mm Hg)
6.2. Diabetes mellitus (treated or known blood fasting glucose >7 mmol/l)
6.3. Current smoking (or smoking stopped within the last 6 months)
6.4. Hypercholesterolaemia (treated or known low-density lipoprotein before the stroke >160 mg/dl or 4, mmol/l)
7. Any condition that prevents long-term follow-up

Date of first enrolment
23/12/2024

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
Netherlands

Study participating centre
Radboud University Medical Center
Geert Grooteplein Zuid 10
Nijmegen
Netherlands
6500 HB

Sponsor information

Organisation
Radboud University Nijmegen Medical Centre

ROR
https://ror.org/05wg1m734

Funder(s)

Funder type
Research organisation

Funder Name
ZonMw

Alternative Name(s)
Netherlands Organisation for Health Research and Development

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date